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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/644,645	08/20/2003	Alan P. Kozikowski	ZAA-003.04	5495

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EXAMINER	
AULAKH, CHARANJIT	
ART UNIT	**PAPER NUMBER**
1625	

DATE MAILED: 03/31/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/644,645	KOZIKOWSKI ET AL.	
	Examiner	Art Unit	
	Charanjit S. Aulakh	1625	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-20* is/are pending in the application.

4a) Of the above claim(s) *7,9,11 and 12* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-6,8 and 13-20* is/are rejected.

7)☒ Claim(s) *10* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *Aug 20, 2003.* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☒ Interview Summary (PTO-413) Paper No(s)/Mail Date. *03/29/04*.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. Claims 1-20 are pending in the application.

Election/Restrictions

2. Restriction to one of the following inventions is required under 35 U.S.C. 121:

I. Claims 1-6, 8, 10 and 13-20, drawn to compounds of formula (I) where X represents –N(Rx)-, pharmaceutical compositions containing these compounds and a method of using these compounds, classified in class 546, subclass 112.

II. Claims 1-20, drawn to compounds of formula (I) where X is other than defined above for group I, pharmaceutical compositions containing these compounds and a method of using these compounds, classified in class 549, subclass 23.

3. The inventions I and II as defined above are patentably distinct, each from the other since they are structurally so divergent that a reference showing compounds of invention I would not render compounds of invention II prima facia obvious. Search required for e.g ; compounds of invention I in class 546 is not the same search required for e.g ; compounds of invention II in class 549 and therefore, constitutes a burdensome search.

4. During a telephone conversation with the applicant's attorney, Mr. Dana M. Gordon on March 29, 2004, a provisional election was made with traverse to prosecute the invention of group I, claims 1-6, 8, 10 and 13-20. Affirmation of this election must be made by applicant in replying to this Office action. Claims 7, 9, 11 and 12 are

withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention. It is of note that group II is subject to further restriction based on the value of variable X in the future applications.

5. Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a request under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(i).

Specification

6. This application does not contain an abstract of the disclosure as required by 37 CFR 1.72(b). An abstract on a separate sheet is required.

Claim Rejections - 35 USC § 112

7. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

8. Claims 14-19 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. The following eight different factors (see Ex parte Foreman, 230 USPQ at 547; Wands, In re, 858.F.2d 731, 8 USPQ 2d 1400, Fed. Cir. 1988) must be considered in order for the specification to be enabling for what is being claimed:

Quantity of experimentation necessary, the amount of direction or guidance provided, presence or absence of working examples, the nature of the invention, the state of the prior art, the relative skill of those in the art, the predictability or unpredictability and the breadth of claims. In the instant case, the specification is not enabling based on atleast four of the above mentioned eight factors such as quantity of experimentation necessary, the amount of direction or guidance provided, presence of working examples, the state of the prior art and the breadth of claims.

The instant compounds are agonists of mGluR2 receptors as demonstrated by the experimental results shown in figure 5 (see page 22, lines 7-11) and therefore, will have utility in treating but not preventing disease conditions where agonistic activity at mGluR2 receptors is of therapeutic benefit. However, there is no teaching either in the specification or prior art references to show the beneficial effect of mGluR2 receptor agonists in any disease condition. There are atleast eight different mGluR subtypes with different pharmacological properties as mentioned in the specification on page 2, lines 4-9. The specification generically mentions role of glutamate receptors in numerous disease conditions. However, there is no mention of specific disease conditions linking to either hyperactivity or hypoactivity of specific subtypes of mGluR receptors. Furthermore, abnormal activity is defined as including decrease or an increase in activation of receptors. It is well known in the art that receptor agonists for any known receptor will have opposite effect to those of the antagonists. There are no working examples to show the effectiveness of the instant compounds in known animal models of any disease condition. The instant compounds of formula (I) encompasses

hundreds of thousands of compounds based on the values of variables R1-R10 and therefore, in absence of such teachings, guidance or presence of working examples, it would require undue experimentation to assess agonist versus antagonist activity of instant compounds at each of different eight subtypes of mGluR receptors, to assess their effectiveness in known animal models of specific disease conditions and hence their utility. In addition, it is well known in the art that there are multiple mechanisms responsible for the etiology of any known disease condition and therefore, correcting one mechanism will not be able to prevent that disease. The instant specification does not teach that hypoactivity of mGluR2 receptors is the only known mechanism responsible for the etiology of all disease conditions.

9. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

10. Claims 1-6, 8 and 13-20 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

In independent claim 1, the term –prodrug—is indefinite since the types of prodrugs and a process for preparing them are not defined. There is not even a single example of prodrug in the specification. The applicants are suggested to delete this term.

In claim 14, the term ---a pathological condition or symptom--- is indefinite since specific disease conditions are not defined. Also, the term ---abnormal activity--- is indefinite

since it is not clear whether hyperactivity or hypoactivity of which specific mGluR receptors is involved out of eight different mGluR receptors.

In claim 19, it is not clear what type of addiction is being reffered here and furthermore, does hypoactivity of mGluR2 receptors is implicated in such addiction?

In claim 20, the term ---detectable label ---- is indefinite since the types of isotopes used as well as a process for preparing specific labeled compounds are not defined.

11. Claims 1-6, 8, 10 and 13-20 are objected as containing non-elected subject matter.

Allowable Subject Matter

12. The following is a statement of reasons for the indication of allowable subject matter:

The instant compounds directed to the elected subject matter are allowable over the prior art since they are neither disclosed nor obvious over the prior art. In the art, Kronthaler discloses mGluR2 receptor agonist, L-CCG I. However, this compound is structurally different from the instant compounds and furthermore, there is no teaching, suggestion or motivation in the art to modify the compounds of Kronthaler to prepare the instant compounds.

13. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Charanjit S. Aulakh whose telephone number is (571)272-0678. The examiner can normally be reached on Monday through Friday, 8:30 A.M. to 5:00 P.M..

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Joseph McKane can be reached on (571)272-0699. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

C. S. Aulakh

Charanjit S. Aulakh
Primary Examiner
Art Unit 1625